Scientists report a breakthrough in stem cell production

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Created cells that match those in ALS patient

By Carolyn Y. Johnson, Globe Staff | August 1, 2008

Reaching a milestone in stem cell research, scientists at Harvard and Columbia universities reported yesterday that they created the first stem cell lines from a sick person, then coaxed these cells to become nerve cells genetically matched to those that had gone bad in a patient's spinal cord.

In a paper published online in the journal Science, the team claimed success at what researchers have long been racing to do: create in the laboratory a plentiful supply of cells that have the same genetic makeup as a patient with a particular disease.

The work was done with patients suffering from ALS, or Lou Gehrig's disease, but the researchers said the same technique can be used to study many other genetic diseases. By comparing diseased cells to normal cells in a Petri dish, scientists hope to better understand what causes disease and test new drugs.

A series of dramatic discoveries over the past two years has pushed stem cell science forward, so this advance was expected. Still, the scientists were thrilled to have accomplished a task that was a fundamental reason for doing stem cell research in the first place.

"Since the cloning of Dolly the sheep and the first derivation of a human embryonic stem cell line by Jamie Thomson some 10 years ago, it's been the hope of scientists . . . to generate stem cell lines that have the genes of a patient," said Kevin Eggan, coauthor of the paper and a principal faculty member of the Harvard Stem Cell Institute. "This really suggests that it's going to be possible to make these cells from patients suffering from other diseases," whether it is Parkinson's disease, diabetes, or genetic heart maladies.

To accomplish their task, Eggan and his colleagues took advantage of a technique developed two years ago by Japanese stem cell researchers that avoids some of the ethical issues that come with embryonic stem cell research. They had planned to create genetically matched stem cells through cloning patients' cells, a process that not only involves some medical risk to women who serve as egg donors, but also requires the destruction of embryos, which some consider the equivalent of murder.

The new technique is much simpler. Researchers insert four genes into a patient's cells, reprogramming them into embryonic- like stem cells. These cells, called iPS cells, appear to have the same capability as embryonic stem cells to develop into any type of tissue in the body.

Eggan and his colleagues created iPS cells from skin cells taken from an 82-year-old ALS patient, then prompted the stem cells to become motor neurons, the type of cells that die off in ALS.

The scientists will study the motor neurons derived from the ALS patient's stem cells, hoping to observe the disease develop in the cells**.** The progressive neurodegenerative disease causes motor neurons in the brain and spinal cord to die, and can lead to paralysis or death. The ALS Association estimates 30,000 people in the United States have the disease.

"It's our lack of understanding of that disease process which is, we believe, preventing us from developing more effective cures," said Christopher Henderson, a coauthor of the paper and codirector of the Center for Motor Neuron Biology and Disease at Columbia University. "We now have in the culture dish cells which have the same genetic makeup as do the ALS patients, and they are the very cells that are affected in the disease. There's no way we could go to an ALS patient and take a sample of their motor neurons."

A more distant goal is to fix defects in the cells and transplant them back into patients, but the technique currently used to create the iPS cells requires adding viruses and genes that can cause cancer.

Jose Cibelli, a professor of animal biotechnology at Michigan State University, said researchers now have a valuable new way to study disease.

"It's one of the papers that is predictable, but until someone actually shows it works, it's up in the air," he said.

The work also shows the overall shift in stem cell research because of political barriers.

When they began working on the experiment more than two years ago, Eggan's team had planned to use somatic cell nuclear transfer, a technique that involves taking human eggs, removing the genetic material inside, and replacing it with genetic material from a patient. Eggan says such work is still crucial, and his laboratory continues to work on that technique, which is considered the "gold standard" for stem cell work. But because of legislation restricting scientists from paying women for their eggs, only one woman has donated her eggs, he said.

The technique using iPS cells "is so much easier, [with] so many fewer restrictions and problems - ethical as well as others," said Rudolf Jaenisch, a stem cell scientist and member of the Whitehead Institute in Cambridge. "I think we'll probably be moving in this direction."

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